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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,291	09/18/2006	Roberto Tonelli	BUG5-38919	4354

86378 7590 02/19/2010

Pearne & Gordon LLP
1801 East 9th Street
Suite 1200
Cleveland, OH 44114-3108

EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
02/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patdocket@pearne.com
dchervenak@pearne.com

Office Action Summary	Application No.	Applicant(s)	
	10/554,291	TONELLI ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9 and 13-15* is/are rejected.

7)☐ Claim(s) *7, 16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Official Action is in response to the papers filed 11/09/09. Any rejection of record in the previous Official Action not repeated herein is withdrawn.

Election/Restrictions

Claims 10-12 and "amino acid carrier" species other than "PKKKRKV" remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and species respectively, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/23/08.

Sequence Rule Compliance

Applicant response filed 11/09/09 provides for sequence compliance.

Priority

Applicant cannot rely upon the foreign priority papers to overcome any rejection in this Official Action because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 recites SEQ ID NO: 1 which is defined in the application to be an antisense PNA (See page 6 of the specification for example). The claim from which claim 2 depends (claim 1) has been amended to embrace only sense PNA molecules. The conflict of the subject matter in claims 1 and 2 provides for an unclear demarcation of the metes and bounds of the claim. The subject matter in claim 2 is in opposite to that recited in the claim from which it depends.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 is drawn to an antisense construct, while claim 1 is limited to sense constructs.

Claims 6, 14, and 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s)

in proper dependent form, or rewrite the claim(s) in independent form. The above claims only recite limitations already required by the claims from which they depend. The claims from which these claims depend already require the claimed invention to be "sense" compounds.

Allowable Subject Matter

Claims 7, 16 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, 8, 9, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sun et al [Peptides Vol.23:1557-1565, 2002, cited by applicant] and Cutrona et al [Nature Biotechnology Vol 18:300-303, 2000, cited by applicants].

The claimed invention is as set forth in the rejected claims.

Sun et al have taught the use of PNA antisense oligomers[12mers and 15mers] with carrier peptides attached to the 3' end of the oligomers where the PNA oligomers target and inhibit N-myc. It has been taught that carrier peptides are beneficial for cell penetration of PNA oligomers. It has also been taught that inhibition of expression of N-myc is desirable to inhibit N-myc for tumor growth inhibition. Sun et al do not teach antigene sequences targeting N-Myc and also do not teach the use of a carrier peptide PKKKRKV.

However Cutrona et al have taught the use of PNA antigene oligomers[sense] for inhibiting a desired gene. The PNA antigene oligomers of Cutrona et al were 17mers and also utilized the carrier peptide PKKKRKV. It has been taught that the use of this carrier peptide facilitates the entry of PNA oligomers into cells. Cutrona also teach the use of PNA oligomers for the inhibition of a target gene to inhibit tumor growth.

The art taken as a whole shows that the instant invention is obvious. The art has shown that it is desirable to inhibit N-myc to inhibit tumor cell growth. The prior art has shown a PNA antisense oligomer inhibiting N-myc expression in cells and has also shown the use of antigen [sense] PNA oligomers for use in inhibiting a desired gene.

The prior art has shown that carrier peptide are beneficial for use with PNA oligomers to facilitate there delivery into cells. The prior art has specifically taught that the peptide carrier PKKKRKV is a peptide carrier that facilitates PNA oligomer entry into cells. The prior art has shown PNA oligomers of various sizes within the recited size range recited in the claims and further it is noted that the size range recited is within the art recognized sizes for the use of antisense applications for target specificity and efficient delivery. One would be motivated to make either antisense or sense PNA oligomers targeting N-myc since the art clearly shows that antisense oligomers targeting N-myc function to inhibit N-myc and since the art has shown that antigen sequences[sense] can also be used to inhibit a desired gene target. One would be motivated to utilize peptide carriers since the art has taught that such carriers are required for effective delivery into cells. One would be motivated to inhibit N-myc since the art has indicated that inhibition of N-myc can inhibit tumor growth.

The invention as a whole would therefore have been prima facie obvious to one in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 11/09/09 have been fully considered but they are not persuasive. Applicant asserts that the sense compounds of their invention have been shown to have improved down regulation as compared to antisense compounds. This in not agreed with for the following reason. The instant specification shows that one particular sense compound inhibited better than one particular antisense compound.

These results are not commensurate in scope with what is claimed. The invention is drawn to any sense compound targeting n-myc where it is not clear that applicants results necessarily translate to the genus of compounds claims. Applicant provides an assessment of the differences of the targets of the prior art and that which is the subject of the instant invention. The prior art teaches inhibition of n-myc via antisense compounds and c-myc via sense compounds (both PNA). It is noted that applicants discussion of the differences of the different targets are not on point for how the references are applied. Sun et al have shown inhibition of n-myc via antisense PNA and have provided motivation to inhibit n-myc. Applicant is directed to page 1557 were Sun et al assert that PNAs provide perhaps the most promising antisense compounds.. On page 1558, first column it has been taught that n-myc, c-myc and l-myc are all related and all are important targets for inhibition. It is also noted by Sun et al that antigene methods have been employed in inhibiting c-myc. At page 1564 it has been taught, in general terms that PNAs can be used to inhibit both translation and transcription. Sun et al, while not specifically employing an antigene method of inhibiting n-myc, clearly indication that PNAs can be used in either method of inhibiting a desired gene target. Now to Cutrona et al who have used antigene methods to inhibit c-myc. This reference should be viewed as explained in the rejection. The teachings of Cutrona et al. For example Cutrona et al assert that their study was intended to explore the conditions that would make anti-gene PNAs effective in intact cells (see page 300, for example). C-myc was chosen to show the general applicability of antigene PNA inhibition. The art taken as a whole doe show that use of PNA as antigene inhibitors

was known in the art at the time of the instant invention. Furthermore it was known to inhibitc-myc via antisense and sense methods. It was known in the art to inhibit n-myc via PNA antisense compounds. The prior art cited in the rejections is related art as evidenced by the discussion of Sun et al in regard to l-myc, c-myc and n-myc. One in the art would surely have looked to the teaching of the cited art and known that one could employ either sense or antisense mediated inhibition of c-myc, l-myc or n-myc.

Claims 2, 7, 16 and 17 are free of the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore can be reached on (571) 272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635

/Sean R McGarry/
Primary Examiner, Art Unit 1635